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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,051	06/08/2000	CHRISTIAN MICULKA	514485-3810	7608

34263 7590 06/27/2005

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,051	MICULKA ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~10/11/00; 11/16/00~~. 8/19/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 46-64 in the reply filed on 19 April 2005 is acknowledged.

Information Disclosure Statement

2. The information disclosure statement filed 11 October 2000 and 16 November 2000 fail to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

3. The information disclosure statement filed 19 August 2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because there is no English copy of the Kemeny non-patent literature nor is there an explanation of the relevance of the literature. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. With regards to non-patent literature EP 0655136, WO 99/45142, and WO 96/35121, only the abstracts have been considered because the bodies of the references are not provided with English translations and there is no explanation as to the relevance of the literature. In addition, Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 47-48, 50-51, and 55-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. In claim 47, line 2, the term "and/or" is vague and indefinite. It is not clear whether both the "capture" and "recognition" sequences (line 2) are claimed, or just one of them.

7. In claim 50, lines 3-4, the phrase "and their active moieties" is vague and indefinite. It is unclear whether the phrase refers only to the "nucleic acids" (line 3) or to all of the limitations preceding the instant phrase.

8. In claim 51, lines 4-5, the phrase "and their 2-amino-4-(carboxymethyl)ribopyranosyl derivatives" is vague and indefinite. It is unclear whether the phrase refers only to the "ribopyranosyluracil" (line 4) or to all of the limitations preceding the instant phrase.

9. In claim 55, lines 2-4, the phrase "the immobilized capture sequence contains various binding sites for the complementary recognition sequence, by means of which various complementary recognition sequences binds to the capture sequence" is vague and indefinite. Since the phrase includes a singular term "the complementary recognition sequence" (lines 2-3) and the plural term "various complementary recognition sequences" (line 3), it is unclear whether the "various binding sites" (line 2) binds to one recognition sequence or multiple recognition sequences.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 46-53 and 55-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al (WO 95/24649) in view of Bolli et al (Chemistry & Biology, 1997).

Ekins et al reference teaches a binding assay in which capture agents 18, 20 are immobilized on a solid support 22 in the form of microspots (i.e. immobilized at defined sites on a carrier), wherein the capture agents are nucleic acid sequences (i.e. at least one immobilized capture sequence) complementary to oligonucleotide tail groups 12, 16 (i.e. at least one complementary recognition sequence), and wherein the oligonucleotide tail groups have antibodies 10, 14 (i.e. antibody binding site for substrate S) attached to thereon and are specific for different analytes 6, 8 (i.e. substrate S). See page 11, line 36 to page 12, line 8; and Figure 1. In addition, Ekins et al teach the steps of exposing analytes 6, 8 to antibodies 10, 14 (i.e. contacting the recognition sequence with sample containing substrate S) and simultaneously or sequentially contacting the analytes and antibodies to the solid support 22 having capture agents 18, 20 immobilized thereon to allow nucleotide sequences 12, 16 to bind to the complementary sequence of the capture agents 18, 20 (i.e. contacting the recognition sequence and sample with the immobilized capture sequence), wherein concentration of analytes is determined using a back-titration technique (i.e. detecting a complex). See page 12, line 10 to page 13, line 2; and Figures 2-3.

However, Ekins et al fail to teach that the at least one immobilized capture sequence and at least one complementary recognition sequence are synthetic and do not bind to naturally occurring nucleic acids.

Bolli et al reference teaches pyranosyl-RNA (i.e. p-RNA; ribopyranoadenosine), in order to provide a stronger and more selective pairing system than RNA and DNA. See page 310, left column, lines 24-29.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of Ekins et al with pyranosyl-RNA, as taught by Bolli et al, in order to provide a stronger and more selective pairing system than RNA and DNA. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including pyranosyl-RNA, as taught by Bolli et al, in the method and apparatus of Ekins et al, since Ekins et al teach capture agents and oligonucleotide tails that are nucleotide sequences, and the pyranosyl-RNA can be substituted for natural nucleotide sequences.

With regards to claims 55-56, Ekins et al teach multiple capture agents having the same sequence within one microspot (i.e. various binding sites) that can bind to a plurality of oligonucleotide tails (i.e. various complementary recognition sequences; at least one further complementary recognition sequence with an additional biomolecule that binds to substrate S). See Figures 1-3.

With regards to claims 58-59, Ekins et al teach that hybridization of oligonucleotide-conjugated antibodies to complementary oligonucleotides is performed with Tris-HCl assay buffer (i.e. salts). See page 16, lines 8-37.

With regards to claims 60-61, Ekins et al teach fluorescent labeling. See page 8, lines 6-10.

14. Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al (WO 95/24649) in view of Bolli et al (Chemistry & Biology, 1997) as applied to claims 46 and 52 above, and further in view of Ribi (US 5,156,810).

Ekins et al and Bolli et al references have been disclosed above, but fail to teach that the capture sequence is immobilized on a carrier electrode of the carrier.

Ribi reference teaches nucleic acid binding members bound to a surfactant layer on an electrode surface, wherein binding an analyte to the nucleic acids perturbs the surfactant layer and produces piezoelectric changes that can be detected, in order to perform sensitive detection of low levels of ligands. See column 1, lines 40-44; column 2, lines 55-68; column 5, lines 59-64; column 8, lines 37-44; column 13, lines 57-66; and column 14, lines 55-60.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Ekins et al and Bolli et al with nucleic acid binding members bound to a surfactant layer on an electrode surface, wherein binding an analyte to the nucleic acids perturbs the surfactant layer and produces piezoelectric changes that can be detected, as taught by Ribi, in order to perform sensitive detection of low levels of ligands. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including nucleic acid binding members immobilized on an electrode surface, as taught by Ribi, in the apparatus of Ekins et al and Bolli et al, since Ekins et al and Bolli et al also teach the immobilization of nucleic acids onto substrate surfaces with detection means to determine analyte binding, and the electrode of Ribi is one type of detection means to determine analyte binding.

15. Claims 62-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al (WO 95/24649) in view of Bolli et al (Chemistry & Biology, 1997) as applied to claim 57 above, and further in view of Sato et al (US 5,187,062).

Ekins et al and Bolli et al references have been disclosed above, but fail to teach that the complex of the recognition sequence and substrate S is in a binding equilibrium, and further comprising isolating the complex after freezing the binding equilibrium.

Sato et al teach the step of freezing coupled antigen-carrier protein after dialysis, in order to store the coupled antigen-protein. See column 5, lines 17-28. Although Sato et al do not explicitly teach isolating the antigen-protein complex, since the complex is placed in storage, isolation of the complex is necessarily required.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ekins et al and Bolli et al with the step of freezing coupled antigen-carrier protein after dialysis, as taught by Sato et al, in order to store the coupled antigen-protein. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including step of freezing the antigen-protein complex and isolating it for storage, as taught by Sato et al, in the method of Ekins et al and Bolli et al, since Ekins et al and Bolli et al teach complex formation, and the freezing and isolating step of Sato et al is performed on a complex.

16. Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al (WO 95/24649) in view of Bolli et al (Chemistry & Biology, 1997) as applied to claim

57 above, and further in view of Sato et al (US 5,187,062) as applied to claim 62 above, and further in view of Cubbage et al (US 5,582,982).

Ekins et al, Bolli et al, and Sato et al references have been disclosed above, but fail to teach the step of covalently cross-linking the recognition sequence and substrate S.

Cubbage et al reference teaches the step of cross-linking nucleic acids and antigens, in order to fix and preserve the ultrastructure of cellular components. See column 5, lines 38-46.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ekins et al, Bolli et al, and Sato et al with the step of cross-linking nucleic acids and antigens, as taught by Cubbage et al, in order to fix and preserve the ultrastructure of cellular components. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of cross-linking nucleic acids and antigens, as taught by Cubbage et al, in the method of Ekins et al, Bolli et al, and Sato et al, since Ekins et al, Bolli et al, and Sato et al teach arrays with nucleic acids and antigens, and the cross-linking step of Cubbage et al is applied to nucleic acids and antigens.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 46-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/899,880. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims include the same limitations.

Claims 46-56 of the instant application recite a recognition system comprising at least one immobilized capture sequence that is synthetic and does not bind to naturally occurring nucleic acids, and at least one complementary recognition sequence that binds to the capture sequence and contains at least one binding site for a substrate S, wherein the recognition sequence is synthetic and does not bind to naturally occurring nucleic acids, wherein the binding of the recognition sequence to the capture sequence forms a non-covalent, hydrogen-bonded molecular pairing system.

Claims 1-12 of the copending application teach a complex comprising an array of microlocations, a pairing component comprising a p-RNA, wherein the pairing component is coupled to at least one of the microlocations, a complementary pairing

component adapted to hybridize to the pairing component, and an immunoreaction binding component coupled to the complementary pairing component.

Although the copending application fails to teach that there can be more than one set of pairing and complementary pairing components, the copending application does teach a complex with an array of microlocations. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include more than one set of paring and complementary pairing components on the complex since the pairing component is coupled to a microlocation, and the claimed complex includes a plurality of microlocations.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. No claims are allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y Lum
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06/10/05